Early diagnosis of dementia

Early Diagnosis of Dementia: Possible Contributions of Neuropsychology

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Introduction

Assessment of the very early stages of senile dementia appears to be of relevance for several reasons. First, it is important to differentiate between "normal" aging and various psychiatric and neurologic diseases, with a view toward possible intervention in the disease process through biological (drugs) and nonbiological (training, psychotherapy) methods. Treatment in an earlier stage of the disease process can be expected to be more successful in view of the less pronounced structural changes. There is some evidence in favor of this hypothesis with respect to treatment with vasopressin-like neuropeptides (e.g., Jolles 1983). Secondly, in the very early stages of senile dementia, the profile of behavioral, emotional, and cognitive deficits the patient exhibits may give some clue as to the cause of the disease or diseases and their pathogenesis.

Unfortunately, diagnostic aids contributing to early assessment are scarce. This paper therefore aims at providing some information on paradigms and methods presently used in assessing dementia and on the kind of insight they may provide on the nature of the aging and dementing process. In addition, the current understanding of behavioral and cognitive dysfunctions in aging and dementia is reviewed.

Neuropsychology of Aging and Dementia

Aging

Recent reviews of cognitive functions in elderly subjects show that there is an age-associated decline in nearly all cognitive functions tested (Jolles and Hijman 1983; Botwinnick 1981), The "normal" aging subject is characterized by a decrease in intellectual functioning, memory, language functions, problem-solving ability, and perception. However, it appears that certain behavioral functions are more affected than others. For instance, old people are not inferior in tasks in which they can rely on well-stored skills and knowledge. Characteristically, aspects of motor performance which have been trained for many years and which have become automatic do not deteriorate as much as the ability to learn new movement patterns. In addition, expressive language does not seem to decline with age. With respect to memory functions, recall memory is affected more than recognition

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memory, indicating that active encoding and retrieval processes are affected more than passive recognition.

Old people perform worse on tasks that require the processing of new information. This is especially the case in situations in which the planning of new activities is important or the active use of coding strategies (e.g., "memory aids") in working memory. The term "mild senescent forgetfulness" is used to describe the developing inefficiency in the consolidation of new information. Characteristic complaints are difficulties in remembering names and recent events and the increasing effort required to remember things which happened many years ago. In addition to this sometimes handicapping memory deficit, there is a tendency towards inflexibility, cautiousness, and conservatism; more effort is needed to change an opinion. With respect to perceptual processes, incoming sensory input seems to persist for a longer period of time and sometimes results in an increased "iconic memory." This "stimulus persistence" interferes with the consolidation of new information: this is a case of the proactive inhibition often seen in elderly people (Botwinnick 1981). The general rate of information processing decreases. This slowness in perception, thinking, and response planning can manifest itself as a memory deficit; when environmental stimuli change rapidly in time, only a limited number can be held in the working memory long enough to be consolidated into long-term memory.

Neuropsychologically, a clear pattern is visible in the cognitive deficits of normal aging. One common element is a link between aspects of cognitive functioning and frontal-lobe functioning. In this view, stimulus persistence, proactive interference, lack of behavioral planning, deficient memory search, and other deficits can all indicate less efficient frontal-lobe functioning (Luria 1973, 1980; Fuster 1980). Interestingly, there is morphological evidence that areas in the frontal lobes degenerate already in people aged 40–50 (Haug this volume). With respect to memory consolidation, limbic areas on the hippocampal and diencephalic levels must be involved (Newcombe 1980; Luria 1980). It remains to be seen whether a general decrease in the rate of information processing is specifically related to the ascending fiber system, according to a hypothesis based on Luria's model of brain-behavior relationships (1973, 1980).

Senile Dementia

No evidence has been found until now that the pattern of cognitive deficits typical of senile dementia of the Alzheimer type (SDAT) is different from that seen in "normal" aging (see Jolles and Hijman 1983), especially with respect to the earlier stages of the dementia. The performance of demented subjects is significantly inferior to that of age-matched controls on all functions tested, but the deficits of the former exhibit no distinct pattern. Thus, more or less profound deterioration is found with respect to perception, memory, language, higher cognitive functions, planning, rate of information processing, and other cognitive functions (Jolles and Hijman 1983; Miller 1981). Along with the deficits seen in normal subjects, SDAT patients also reveal diminished capabilities with respect to recognition memory and verbal IQ measures, which stay at a fairly constant level in nor-

mal aging. Interestingly, clear differences seem to exist in the pattern of cognitive deficits seen in other types of dementia. For instance, the (pre) senile dementia of the Pick type shows especially pronounced behavioral disturbances and deficits in the planning and organisation of behavior. These deficits are characteristic of dysfunctions of the frontal lobe. Incidentally, these frontal signs are much more pronounced than in the normal aging process which was discussed in the preceding section. This neuropsychological interpretation is in line with current knowledge on the cerebral substrate of Pick's disease, which appears to be a fairly specific degeneration of frontal lobe areas (see Strub and Black 1981). In addition, those dementias arising primarily from vascular disorders (multi-infarct dementia) can in principle be differentiated from SDAT because there is more evidence for focal deficits. (For example, a patient revealing modality-specific deficits for complex visual material and spatial disorientation, though no memory deficit for verbal material, almost certainly does not suffer from a primary degenerative dementia, but may have had an infarct confined to right-hemisphere structures).

It has been suggested that the behavior typical of the various SDAT stages may parallel comparable stages of neuroanatomical degeneration (Jolles and Hijman 1983). More specifically, the temporal sequence of the development of cognitive deficits in SDAT suggests that there might be a degeneration of association areas in the neocortex occurring as a result of the degeneration of ascending fibers projecting to the neocortex. This hypothesis is primarily based on the observation that subjects in the very early stages of dementia do not show neocortical – higher cognitive – deficits, but do show consolidation deficits (limbic system) and slowness (ascending fibers). After degeneration of the higer-order, non-modality-specific association areas (see also Luria 1973, 1980), a further degeneration affects the sensory association areas, whereas the primary sensory projection areas stay relatively intact until very late in the disease process. This appears from the fact that aphasia, apraxia, and agnosia (behavioral manifestations of cortical involvement) develop in later stages of the disease process. Furthermore, ability to perform simple motoracts is preserved (activity of the primary motor cortex and premotor area). Likewise, severely demented patients are still capable of the use of syllables and phonemes (but not words) in undirected babbling. Support for this neuropsychological hypothesis comes from histologic investigations providing evidence that several cortical areas remain relatively intact during the course of the disease (Brody and Vijashankar 1977; Hanley 1974) and from the correlation between the extent of cortical degeneration (number of senile plaques) and poor test performance (Blessed et al. 1968).

Methods of Early Assessment

Psychometry

Generally, standard tests have increased our knowledge of how deficits develop in normal aging and dementia. Unfortunately, although this knowledge has been applied to groups of elderly subjects and patients as a whole, no psychometric

tests appear sensitive and reliable enough to be used in the early assessment of disorders in individuals. The advantages of psychometric tests are that they are standardized and that published norms are generally available. In addition, they are easy to administer and usually have good reliability.

A general drawback of the psychometric approach is that the use of test scores does not necessarily make it possible to identify the cognitive deficits that underlie the performance changes. Traditionally used tests allow only a fairly crude estimation of cognitive functions and, in addition, do not properly differentiate between different aspects of these functions. This is a consequence of the empirical, nontheoretical nature of these tests, which have been developed for purposes other than for use with brain-damaged subjects. For example, the Digit-Symbol subtest of the Wechsler Adult Intelligence Scale (WAIS) is the most sensitive among the 11 subtests, showing the greatest difference between the performance of young and old adults (Botwinnick 1981). However, it is not clear whether psychomotor slowing, poor learning or retrieval of the digit-symbol codes, poor visual motor coordination, or all of the above are responsible for the poor performance of aged subjects (Poon 1983).

The psychometric test measure thus gives a quantitative index of below-average performance, without any clue as to the nature of the cognitive deficit and the underlying cerebral substrate. In other words, psychometric tests generally measure performance and not cognitive functions. Consequently, they do not allow a proper differentiation of different aspects of these functions, and this limits their use both in the assessment of the early stages of senile dementia and in differential diagnosis.

A second drawback of the traditional psychometric tests is the relatively long time needed for test administration, when compared with the amount of data that the test or test battery yields. For instance, the administration of the WAIS takes several hours and yields only 11 (subtest) scores when the test are used in the classic way. These scores are usually converted into two scores for Verbal IQ and Performal IQ, which are often combined to yield the total IQ. Another test battery, the Halstead Reitan Neuropsychological test battery (HRNTB; administration in 5–6 h, has the drawback that standard norms are available for subjects up to 55 years of age, but not for older subjects.

Apart from the use of standardized test batteries (HRNTB, WAIS, the Nebraska battery), several more specific psychometric tests are used for the determination of deficits in aging and dementia, especially those concerning aspects of memory processes (see Jolles and Hijman 1983). Characteristically, the resulting quantitative data are used for the analysis of group differences (e.g., "young" versus "old" adults). Generally, the quantitative results do not lend themselves to use in individual diagnosis, especially in distinguishing early dementia from other syndromes. More recently, there has been some movement toward using psychometric tests and test batteries in a less rigid and more qualitative way (e.g., Lezak 1983; Goodglass and Kaplan 1979). Proponents of such an approach use quantitative results and more qualitative signs; however, no published data are available as yet on the use of this new approach in the early diagnosis of senile dementia (see "Behavioral and Cognitive Testing: An Integrated Approach" below).

Information Processing

Investigations of cognitive processes in the psychological laboratory have generally made use of an information-processing paradigm. The strength of this approach is the theoretical framework, which attempts to examine cognitive processes by analyzing behavior in terms of quantifiable components and qualitative patterns. Information-processing tasks are characteristically broken down into subtasks, and reaction time measurements are used to probe into the different stages of information processing (e.g., Brand and Jolles 1985).

The use of information-processing tasks developed in the psychological laboratory and later adapted for use in clinical testing is still in its infancy. The Sternberger Memory Comparison Task (Sternberg 1975) which has been used extensively in the laboratory, has been employed in group comparison studies and to determine the efficacy of drug trials but not in psychodiagnosis on an individual basis. However, a recently developed paper-and-pencil version appears to be a reliable and sensitive task which can be combined with clinical neuropsychological tests (Jolles and Gaillard 1985). Data obtained with this test suggest that the intercept of the Reaction-time – Set-size function increases with age. This suggests that aging is associated with a decreased rate of perception and motor performance (Jolles and Hijman 1983), but has no effect on the rate of memory search. However, an increased slope in demented subjects characterized by some aspects of frontal lobe dysfunctioning suggests a fairly specific effect on search processes.

Other information-processing paradigms have been recommended for use in geriatric psychopharmacology (Poon 1983). These methods might also be of importance in the clinical assessment of subjects suspected of suffering from incipient dementia. According to Poon, these paradigms assess common behavioral complaints both in community-dwelling elderly and in elderly patient populations. Large amounts of data have been obtained on speed, accuracy, and response patterns, expecially with respect to the following functions: ability to attend and concentrate, to make dexisions quickly, to acquire and retrieve new information, to retrieve familiar information (naming), and to manipulate spatial information. It is again important to note that inferences are made with respect to aspects of cognitive functioning through the use of reaction time measurements. Poon (1983) recommends and describes the following procedures for use in geriatric assessment: (a) measurement of the alerting function to assess attention/arousal; (b) measurement of choice reaction time to assess decision-making processes; (c) measurement of continuous recognition memory to assess retrieval from primary and secondary memory; (d) measurement of naming latency to assess retrieval from tertiary memory; (e) measurement of mental rotation to assess spatial processing. A detailed description and rationale of these preedures can be found in Poon (1983).

It is of interest to note that several psychometric tests which have been in clinical use for several decades can be used as an information-processing task: One example is the Stroop test (see Lezak 1983), which consists of three subtasks measuring (a) the speed at which color names are read, (b) the speed at which colors are named, and (c) the speed at which the color of printing ink is named

when there is interference from the printed color name. An interference score can be calculated by subtracting the time scores 3–2. This is a relatively pure index which is not contaminated by a perceptual or motor component. A similar procedure can be performed with the Trail-Making test (see Lezak 1983). The subtraction of time scores gives a timed measure for the ease with which a concept shift is made (here, shifting between letters and digits, Vink and Jolles, in preparation).

Behavioral Neurology

A different approach toward assessing cognitive functioning relevant to geriatry has been developed by the Russian neuropsychologist A. R. Luria, who has elaborated a model of brain-behavior relationships to serve as a basis for an extensive neuropsychological investigation. His approach consists of a set of procedures which systematically assess the different aspects of cognitive functioning. The method Luria developed, which has become known in the adapted version of Christensen (1975), is qualitative and flexible in nature:

1. Motor functions
   - simple movements, dynamic organization
   - oral praxis
   - speech regulation of the motor act
2. Acoustico-motor organization
   - perception and reproduction of pitch and of rhythmic structures
3. Higher cutaneous and kinesthetic functions
   - cutaneous, muscle, and joint sensation
   - stereognosis
4. Higher visual functions
   - visual perception
   - spatial orientation
   - intellectual operations in space
5. Impressive speech
   - phonemic hearing
   - word comprehension
   - simple and complex grammar
6. Expressive speech
   - articulation
   - reflective speech
   - nominative speech
   - narrative speech
7. Writing and reading
   - word analysis and synthesis
   - writing
   - reading
8. Arithmetic skills
   - comprehension of number structures
   - arithmetic operations

9. Mnestic processes
   learning processes
   retention and retrieval
   logical memorizing
10. Intellectual processes
   thematic pictures and texts
   concept formation
   discursive intellectual activity

According to this method, more than 250 simple tasks are given to the subject, ranging from tests for simple and complex motor acts and perceptual, language, and memory functions to tests for higher cognitive functions. Total administration time is 1–2 h. In essence, Luria's method aims at generating hypotheses concerning specific disabilities and testing these hypotheses by a proper choice of small tasks. For instance, with respect to memory functions, he discerns between memory for visual forms ("draw the figures that you saw") and verbal material ("write the words you saw"). Both the learning performance and the sensitivity to interference by homogenous or heterogenous material are measured (e.g., remembering three words after "interference" in the form of three other words or a visually presented scene). In addition, the formation of a stable intention to memorize or to associate is assessed in addition to several other aspects of memory (Luria 1976). Luria used his method originally in the examination of brain-injured subjects, and the tests have provided important information in assessing the location of brain injuries and in planning rehabilitation programs. More recently, it has appeared to be effective in determining "functional" psychiatric illness of "organic" patients (Purisch et al. 1978) as well as in the assessment of SDAT (Ernst et al. 1970; Sulkava and Amberla 1982; see "Stages in Dementia" below).

Luria's investigation is essentially an example of behavioral neurology. The administration of the tasks is systematic but nonstructured. Its main advantage is the fact that the assessment schedule is based on a theory of brain-behavior relationships, thus making it possible to offer an interpretation with respect to the aspect or part of a functional system affected. This approach gives rise to a wealth of data which has more coherence than the data derived from a battery of standard psychometric tests. A main disadvantage of the procedure is its qualitative nature, which necessitates extensive training and reduces interobserver reliability. In addition, the lack of quantifiable data prohibits the use of the paradigm in the assessment of treatment efficacy or of cognitive decline in individual subjects. However, used in combination with psychometric tests and information-processing tasks, it can provide important information on the selective nature of cognitive defects in elderly subjects and SDAT (see "Behavioral and Cognitive Testing: An Integrated Approach"). Recently, attempts have been directed at quantifying the results of Luria's neuropsychological investigation. Unfortunately, the Luria-Nebraska battery (Golden et al. 1979), a structured and semiquantitative test series, has lost the flexibility and richness of the original method, in addition to having several other shortcomings (Adams 1984 and several references cited there).

Behavioral and Cognitive Testing: An Integrated Approach

Because the psychometric, the information-processing, and the behavioral-neurological approaches all have their strengths and weaknesses, it may be more fruitful to use them in combination for the early assessment of SDAT and related disorders. The assessment procedure used for this purpose in our clinic is a combination of a qualitative behavioral-neurological examination and quantitative methods derived from psychometry and information-processing paradigms. The procedure is first to get a qualitative impression of the total range of cognitive functions (see p. 89). When signs indicating a possible deficit are revealed, a more detailed investigation is carried out to explore them further. Other qualitative tests are employed in order to determine whether there is indeed a deficit and to ascertain its specific nature. These tests are then followed by quantitative methods which "measure" the deficit and relate it to existing norms. This approach has several advantages. First, it is possible to make a profile of a broad range of cognitive functions. For instance, it is fairly easy to indicate the aspects of cognition which reveal no deficits. Second, the numerous observations increase the reliability of the eventual interpretation. Third, the duration of the neuropsychological investigation has been decreased as a result of the relatively shorter duration of the qualitative tests. Fourth, hypotheses based on a thorough knowledge of brain-behavior relationships are tested. Finally, much emphasis is given to pathognomonic signs, or clear signs of existing pathology. The psychometric tradition does not usually pay attention to these signs.

The test series used to assess early dementia in our clinic consists of the following tests and tasks: (1) the Luria-Christensen test battery described above; (b) a 15 word learning test giving information on the use of active coding strategies, consolidation versus retrieval, rate of retrieval, and sensitivity to interference (Luria 1976; Brand and Jolles 1985); (c) the Utrecht memory comparison task evaluating rates of perception, motor output, and memory comparison (Jolles and Gaillard 1985), (d) the Stroop Interference task (naming; retrieval of words, and color names, color-word interference; Lezak 1983); (e) the adapted version of the Trail-Making test (rate of perception, retrieval of letters, and flexibility in concept shifting; Lezak 1983); (f) the Road Map test (left-right discrimination, evaluation, mental rotation; Lezak 1983); and (g) the Symbol-Digit Modalities test of general speed of perception and motor output, Lezak 1983). In addition to this test series, a variety of other tests explore any specific deficits found more deeply. These tests are either chosen from standard batteries (e.g., tapping test from HRNTB or the block design test of the WAIS) or consist of experimental tasks used in an ad hoc fashion (e.g., experimental tasks designed to assess decision speed, tactile functions or the dichotic listening task).

Luria used syndrome analysis as a means of describing the profile of cognitive strengths and weaknesses in his subjects. Specifically, the syndrome he described appears to involve particular brain structures, for instance, the frontal areas, as seen in deficits relating to many different functional systems, such as perseveration in motor function, proactive memory interference, a flat learning curve on a word-learning test, and disabilities in shifting concepts among others. A similar syndrome analysis also appears to be important in conjunction with test methods

such as those described here, enabling a profile of a subject's cognitive strengths and weaknesses at a given moment to emerge. A profile analysis of this type is an attempt to simplify a picture which might otherwise contain too much information to be intelligible. Examples of this approach are discussed in "Neuropsychological Contributions to Differential Diagnosis" below. Interestingly, the large amount of data gathered per individual subject appears to make possible a fairly reliable description of individual cases.

Neuropsychological Contributions to Differential Diagnosis

Reactive Depression Versus (Pre)senile Dementia: Case Studies

The approach described in the preceding paragraph is illustrated in the following description of a neuropsychological examination of two elderly patients. The first, a 63-year-old man, was referred to us for treatment of memory deficits and had been hospitalized for several years in a psychiatric clinic. He was diagnosed as suffering from a depression with "theatrical, hysteria-like character neurosis." He sometimes manifested bizarre behavior; both nurses and spouse complained about his tendency to "attract attention." The patient himself complained of occasional memory lapses for complex behavioral activities such as dish-washing and setting the table. He was afraid that he was suffering from incipient dementia and felt depressed about his decreasing capabilities. A neuropsychological examination provided the following information:

A normal conversation was possible, although the patient was fairly passive in his response towards instructions. Speech was adynamic and there was some inertia of movement. Intellect and consciousness were not overtly disturbed. Behavioral-neurologic investigation showed no particular deficits in simple or complex motor functions, except for a slight tendency to persevere on a movement pattern (for example, tapping four times when three times had been requested). Auditory, visual, and tactile perception were normal. However, he clearly manifested proactive interference suggestive a frontal cortex dysfunctioning according to Luria (see above discussion). A more clearcut perseveration was seen on the Luria Meander (Fig. 1, part A), a pattern capable of eliciting any tendency to persevere. The patient still manifested this perseveration several minutes later; the movement pattern of the meander appeared to interfere with the requested performance of a new motor pattern (Fig. 1, part B). Interestingly, another aspect of perseveration was seen on a higher cognitive level. The subject was requested to draw a simple figure from memory (Benton test; Fig. 1, part C). When similar tasks were set later (Fig. 1, parts D and E), there was a clear persistence of the movement and visual pattern belonging to the earlier task (Fig. 1, part C) that interfered with later stimuli. On quantitative tests such as the trail-making test, a fairly normal performance was seen on the first subtask, but the subject was much too slow on the second subtask and also made several errors. Consequently, there was a lack of flexibility without a general decrease in the rate of information processing. With respect to memory functions, imprinting appeared fairly normal

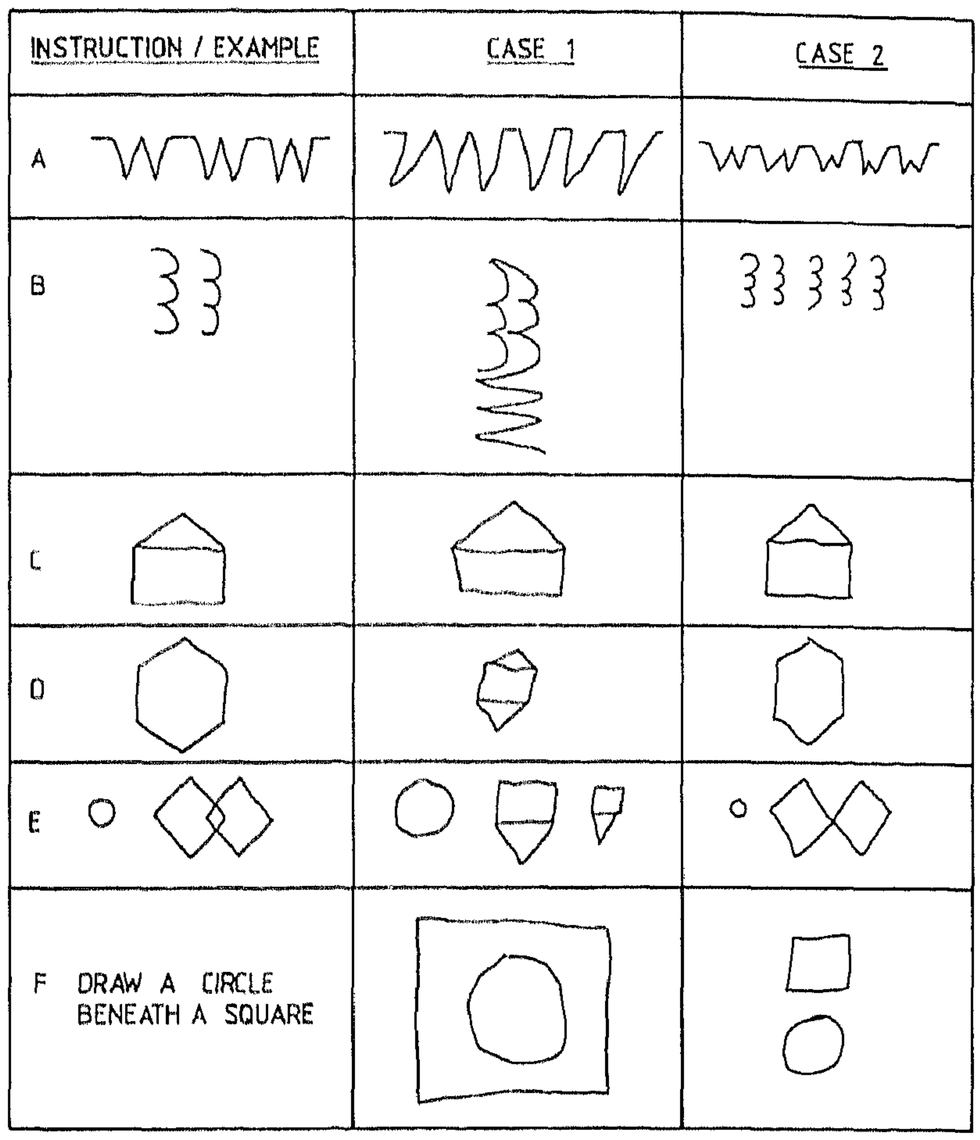

Fig. 1 A–F. Comparison of neuropsychological test results of two elderly subjects with depression, suspected of possible senile dementia

(recognition memory), but a flat learning curve was noted in a word-learning test: the subject encoded the material passively and in a fairly stereotyped manner, indicating that active encoding and active retrieval from memory was disturbed. Finally, with respect to language functions, vocabulary was normal, although one specific language disorder was present. Words used to describe relations in language (for instance, "because," "as," "if," "then," "greater than") appeared not to be understood. Part F of Fig. 1 shows how the instruction to "draw a circle beneath a square" was carried out in correctly. "Beneath" was interpreted in a concrete, three-dimensional fashion, whereas all normal elderly subjects would have drawn "beneath" according to a two-dimensional conception. The patient also failed on several other tasks in which similar logical relations in language had to be expressed. The performance of the other subject (case 2) was normal (Fig. 1).

Recapitulating, it appears that the subject had severe deficits in the planning and organization of complex behavioral acts. No clearcut disorder of perception, memory, and simple language functions and no general slowness were observed. It was concluded that the patient had a dysfunction of the frontal neocortex, particularly of the lateral surfaces, as indicated by the patients general inertia. A computerized tomography scan performed later has shown some central and peripheral atrophy, frontally more than posteriorly. The EEG was diffusely irregular. An early stage of Pick's disease was a possible diagnosis, although other causes of impaired frontal lobe functioning could not be excluded. A follow-up investi-

gation will be undertaken at a later stage to asses whether there is further deterioration.

The other subject (male, 72 years of age) was referred to us because of persistent depression, failing memory, and possible early dementia. The subject was very sharp, with adequate responses and sometimes initiated the conversation. He complained of memory lapses and the fact that all his actions required so much energy. No pathognomonic signs appeared in the behavioral-neurological examination (Fig. 1), although he was very slow in performing complex acts of manual dexterity. His attention span appeared to be short, and automatic acts were performed in a controlled and time-consuming fashion slower than normal for his age. When given the time, his performance on many tests – including memory tests – was normal. No planning deficits and language deficits were seen, but there was a clear deficit in visuoconstruction and in performance on a test measuring mental rotation.

It was concluded that the scores of memory tests were not low enough to warrant a diagnosis of early dementia. In addition, there was no indication of specific frontal involvement. This profile of slowness and visuoconstructive deficits is often seen in certain subgroups of depressive patients. The neuropsychological examination of the two seemingly similar subjects thus gives rise to a strikingly different conclusion as to the nature of the underlying disorder and the cerebral substrate involved. The depression of the first subject is almost certainly secondary to some kind of dementia which is especially dependent on frontal cortex functioning. The second subject is depressed and not demented manifesting cognitive deficits more often seen in depression which might be mistaken for signs of dementia. The interpretations are based on a combined analysis of data obtained in the behavioral examination and the preliminary conversation (hypothesis generation). Indications of pathognomonic signs were discovered in the behavioral-neurological examination, while speed and other parameters were measured in psychometric and information-processing tasks. It is the combination of these modes of investigation which gives rise to the specific profile of deficits.

Stages in Dementia

A very important objective in the early assessment of dementia is the differentiation of "normal" aging from early dementia. The deficits accompanying normal aging are relatively mild; for instance, some mild frontal lobe signs corresponding to mild senescent forgetfulness develop, manifesting themselves as a deficit in active encoding and retrieval (see "Neuropsychology of Aging and Dementia"). However, a clear consolidation deficit is not seen in normal elderly people, in contrast to the early stages of dementia. A profile analysis of one individual illustrates this point (Fig. 2). The subject referred to here (female, 64 years of age) was normal in several different cognitive functions (higher language functions, arithmetic, simple perception, and simple motor functions). However, a very profound memory defect was evident, especially in the learning and retention of new material, resulting in a total inability to recall words learned 30 min earlier. In addition, passive recognition of words was also inferior to normal, indicating a con-

solidation deficit. The rate of information processing was moderately decreased. The dynamic organization of hand movements was much less efficient (e.g., the rapid alternation of movements between left and right hand or the smooth succession of different movement patterns with one hand, especially when hand movements had to be accompanied by speech acts). A very relevant finding was a gradual deterioration of memory functions and speed at a follow-up examination conducted 1 year later, while several other functions revealed no decreases. It appears that the various cognitive deficits may develop successively over time. The CT scan of this subject was normal (atrophy conforming to age), and she was tentatively diagnosed as suffering from DAT.

Figure 2b shows the cognitive profile of a 59-year-old man whose memory deficits differ strikingly from those of the subject just described in that he exhibited more retrieval deficits than consolidation deficits and a degree of disordered memory secondary to planning disorganization. In addition, general slowness together with fairly good consolidation was evident, while impressive speech faculties and dynamic organization were far inferior to the performance of the female subject just discussed. Follow-up assessment after 0.5 and 1 year corroborated the first impression of primary degenerative dementia of the frontal type. A CT scan conducted 6 months later showed some sulcal enlargement and widened interhemispheric fissure, especially in the frontal lobe. The atrophy was more pro-

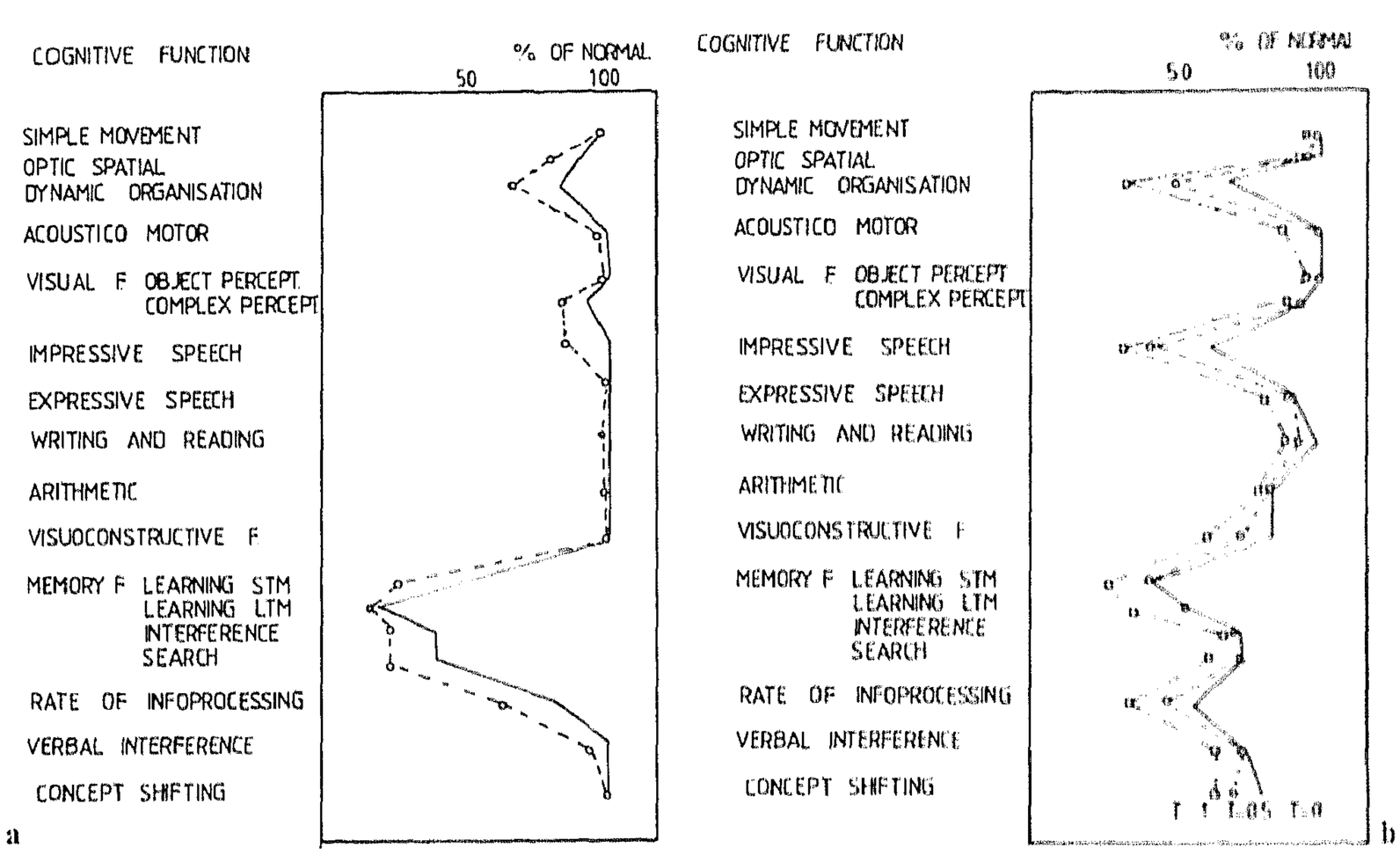

Fig. 2a, b. Neuropsychological profiles of two elderly subjects. The neuropsychological profile is drawn for the cognitive functions measured by the test series described in the text. The individual qualitative tests were scored on an ordinal scale (0–2) and converted into mean scores for a specific function. Four functions (memory, rate, interference, and shifting) are based on quantitative data. The relative performance as compared with age-matched controls is given. **a** Subject (female, 64 years) was assessed two times; at $T=0$ (——) and $T=1$ year (– – –). **b** Subject (male, 59 years) was assessed three times, at $T=0$ (——), $T=0.5$ year (– – –), and $T=1$ year (. . . .)

nounced 1 year after the first examination, which is in line with the interpretation based on the neuropsychological examination.

Further studies have been performed with larger groups of subjects who have, however, not been tested more than once. The general findings conform to those obtained by Sulkava andd Amberla (1982) in a study with the Luria-Christensen neuropsychological test battery. These investigators found that different phases in the development of dementia can be discriminated, even at the later stages. Both presenile and senile patients exhibited pronounced deterioration of orientation, memory and higher cognitive, visual, and motor functions. Impressive and expressive speech were relatively spared. All functions deteriorated gradually during the disease process, so that the differences between the various abilities and the slope of the performance profile were preserved. All neuropsychological abilities tested had disappeared by the final phase (Sulkava and Amberla 1982).

According to these authors, both the presenile and the senile form of DAT seem to follow a clearly definable course affecting different functions of the brain in a certain order. Symptoms such as a general diminishing of activity or deterioration of short-term memory and of awareness appear at an early stage of the disease. Consequent behavioral dysfunctions are disorientation and paranoid delusions. Theoretically, this may indicate that fibers ascending from the brainstem to the cortex are affected (see "Neuropsychology of Aging and Dementia"). In the next phase, apraxia, agnosia, and aphasia disorders appear, together with deterioration of logical reasoning and loss of control over behavior (i.e., indicating cortical involvement). In the advanced stages of the disease, only a few basic functions (e.g., automatisms) may still be preserved (Sulkava and Amberla 1982; Jolles and Hijman 1983). The data indicate that a neuropsychological examination based on Luria's brain-behavior model, coupled with a profile analysis, yields information of relevance both to early assessment of the disorder and to increasing knowledge not only of the succession of stages in DAT, but also – indirectly – of the cerebral substrate involved.

Dementia Versus Psychiatric Disorders

(Neuro)psychologists working in a psychiatric setting are frequently asked to assess whether a particular patient is demented or not, as it is very difficult to differentiate the early stages of senile dementia from depression. On the one hand, early stages of dementia are very frequently accompanied by a depressed mood (Jolles and Hijman, 1983; Strub and Black 1981), which is most probably a reaction to the subjective realization of suffering cognitive deterioration (cf. the first case study in "Reactive Depression versus (Pre)senile Dementia"). Incidentally, there is evidence that the major catecholaminergic pathways believed to be involved in depression (Van Praag 1982) play a similar role in the pathogenesis of SDAT (Rossor 1982), thus suggesting that there is – at least in part – a common cerebral substrate in both depression and dementia. On the other hand, profoundly depressed patients frequently display overt signs of dementia such as slowness, general inertia, disorientation, and memory disturbances. The differentiation of depression and dementia based on clinical observation alone thus ap-

pears very difficult. A thorough neuropsychological examination may be of importance in this respect.

Recently, a group of 29 depressive inpatients from the university psychiatric clinic were subjected to such an examination to determine whether any members of the group had been misclassified as demented (Jolles and Brand, in preparation). After neuropsychological analysis, it was possible to discern seven subgroups. Groups 1–6 had a fairly specific profile of cognitive deficits that could be used as a basis for making distinctions among them. Group 7 ("others") consisted of six different profiles which did not resemble those of any of the other subjects. Interestingly, these six subjects had had life events which were suggestive of some brain disease, thus explaining the specific pattern of deficits (two subjects with brain trauma; one with hysteric conversion, one with migraine, and two postanoxic subjects). Group 1 (two subjects) manifested only some nonspecific cognitive deterioration without any deficits relating to memory, motor functions, planning, or automaticity. Group 2 (six subjects) had similar nonspecific deficits as well as deficits in automatism and memory retrieval. Group 3 (six subjects) was very different, in that these subjects, in addition to the deficits characterizing group 2, were also very slow, manifesting some motor and higher cognitive perseverations or perceptual changes. Group 4 (three subjects) was similar to group 3, but also showed memory consolidation deficits. The extremely profound deficits of the patients in groups 3 and 4 suggest that they suffer from retarded depression. Groups 5 and 6 manifested clear-cut signs of brain dysfunctions. Group 5 ($n=2$) exhibited no slowing of actions but had especially pronounced motor dysfunctions suggestive of frontal cortex involvement. Group 6 ($n=3$) was characterized by subjects with profound cognitive and behavioral deficits in all cognitive functions measured. When these profiles are represented schematically, they suggest that group 6 consisted of demented subjects. One subject of this group later turned out to have multi-infarct dementia, while another subject suffered from lupus erythematosus. Long-term follow-up will make it possible to monitor groups 3 and 4. Until now, several subjects from groups 1–3 have evidenced some improvement of cognitive deficits, accompanied by an alleviation of their depression.

Besides depressive patients, another group of psychiatric patients can be distinguished from demented subjects only with difficulty. In view of the important role of the frontal lobe in behavioral planning and organization, dysfunctions of the frontal lobe or structures within it can easily manifest themselves as disorganized and bizarre behavior. This might thus be misinterpreted as a "functional" psychiatric disorder. The patients referred to in Figs. 1 and 2 and in group 5 are examples of such patients. It is interesting to note that most patients with Pick's disease die in a psychiatric hospital. It will be of more than scientific interest to explore how many psychiatric patients are in fact misclassified because they have deficits in behavioral planning and organization which – until now – have not frequently been recognized as an indication of frontal lobe involvement or as signs of a specific type of degenerative dementia.

Conclusion

Some evidence has been presented to show that most of the methods which have until now been used in the assessment of early stages of dementia have their drawbacks. It appears that the use of a *combination* of psychometric tests with techniques based upon information-processing paradigms and behavioral neurology may be the most fruitful approach. Future developments will almost certainly be in the direction of techniques that are more sensitive and capable of giving more insight into the nature of the cognitive deficits. Information-processing tasks such as those proposed by several authors (Poon 1983; Brand and Jolles 1985) will contribute, provided that some relation is made between cognitive functions and the underlying cerebral substrate, and provided that tasks are constructed which have ecological validity.

The neuropsychological profile analysis (Figs. 1, 2) illustrated here does no more than indicate a possible method for analyzing data. It is clear that a description purely in terms of test results is too crude to describe the complexity of an individual's pattern of cognitive strengths and weaknesses. Similar developments can be seen in psychiatric diagnosis. For example, the Present State Examination (Wing et al. 1972) and the Geriatric Mental Scale (Copeland, this volume) also use some kind of profile analysis in the description of psychiatric symptoms. The neuropsychological profile analysis proposed here is based on a model of brain-behavior relationships (i.e., the model of Luria). It is important to simplify the large amount of data into a smaller number of categories. A good brain-behavior model provides a rationale according to which this may be done.

With respect to the potential contributions of neuropsychology, several points are of interest. In the first place, modern neuropsychology is a neuroscience when it tries to relate behavioral and cognitive functions to the underlying cerebral substrate. A model such as that put forward by Luria presents a working hypothesis which is essential if aspects of behavior and cognition which would otherwise never have been suspected of containing common elements are to be related (see, for instance, the different aspects of frontal involvement). A model of DAT based on neuropsychological theory predicts that the evolution of behaviorally observable deficits in DAT may initially be a manifestation of an underlying degeneration of ascending fibers, followed by progressive atrophy of nonspecific hippocampal and sensory neocortical association areas and neocortical sensory association areas (see "Neuropsychology of Aging and Dementia" and Jolles and Hijman 1983).

Another theoretical contribution concerns the findings that – based on neuropsychological examination alone – there are no qualitative, but only quantitative differences between aging and DAT (Jolles and Hijman 1983) and between the presenile and the senile forms of DAT (Sulkava and Amberla 1982). Human neuropsychology may thus provide testable hypotheses which will deepen our insight into the nature of the underlying disease and its cerebral substrate.

A second relevance of neuropsychology concerns the implications which emerge from a better behavioral and cognitive description of the deficits. For instance, elderly individuals seem to lose the ability to retrieve information consolidated in the past. A consolildation deficit is especially evident in dementia. Might

it not be the case that the real underlying deficit is a decreasing ability to cope with environmental stimuli and that mechanisms for handling new information are unused and thus atrophy? This notion could motivate changes in society allowing older people increased opportunities to engage in new activities and actively plan their own lives. Presently, there is a tendency in exactly the opposite direction, namely to take responsibility out of the hands of the elderly. This is especially true in psychiatric institutions. Patient rehabilitation and training based upon neuropsychological theory would prescribe training in order to compensate for lost capabilities. In this respect, much emphasis must be given to activating behavior planning as opposed to passive perception. The strategy of an "enriched" environment, which is known to have beneficial effect on cortical thickness and neuronal connections in animals, might have similar effects in man.

Analogous to the muscular atrophy that develops in a disused broken leg, brain atrophy may result from a lack of interaction between the organism and its environment. This atrophy might – theoretically – be reversible if noted in the very early stages. A stimulative therapy of the type suggested here, possibly in combination with newly developed drugs (e.g., neuropeptides), might be the treatment of choice in elderly people who are at risk of becoming demented.

References

Adams KM (1984) Luria left in the lurch: unfulfilled promises are not valid tests. J Clin Neuropsychol 6:455–458

Blessed G, Tomlinson BE, Roth M (1968) The association between quantitative measures of dementia and of senile changes in the cerebral grey matter of aged subjects. Br J Psychiatry 114:797–811

Botwinnick J (1981) Neuropsychology of aging. In: Filskov SB, Boll TJ (eds) Handbook of clinical neuropsychology. Wiley, New York, pp 135–171

Brand N, Jolles J (1985) Memory scanning and response requirements (to be published)

Brody H, Vijashankar N (1977) Anatomical changes in the nervous system. In: Finch CE, Hayflick L (eds) Handbook of the biology of aging. Van Nostrand, New York

Christensen AL (1975) Luria's neuropsychological investigation. Text, Munxgaard Copenhagen

Ernst B, Dalby MA, Dalby A (1970) Luria testing in demented patients. Acta Neurol Scand [Suppl] 43:97–98

Fuster JM (1980) The prefrontal cortex. Raven, New York

Golden CJ, Hammeke TA, Purish AD (1979) The Luria-Nebraska neuropsychological battery manual. Western Psychological Services, Los Angeles

Goodglass H, Kaplan E (1979) Assessment of cognitive deficit in the brain-injured patient. In: Gazzaniga M (ed) Handbook of behavioral neurobiology, vol 2. Neuropsychology. Plenum, New York

Hanley T (1974) Neuronal "fall-out" in the aging brain: a critical review of the quantitative data. Age Aging 3:133–151

Jolles J (1983) Vasopressin-like peptides and the treatment of memory disorders in man. Progr Brain Res 60:169–182

Jolles J, Gaillard AWK (1985) A paper and pencil version of the Sternberg memory Comparison Task (to be published)

Jolles J, Hijman R (1983) The neuropsychology of aging and dementia. Dev Neurol 7:227–250

Lezak MD (1983) Neuropsychological assessment, 2nd edn. Oxford University Press, New York
Luria AR (1973) The working brain. Penguin, Harmondsworth, UK
Luria AR (1976) The neuropsychology of memory. Winston, Washington DC
Luria AR (1980) Higher cortical functions in man, 2nd edn. Basic, New York
Miller E (1981) The nature of the cognitive deficit in dementia. In: Miller NE, Cohen GD (eds) Clinical aspects of Alzheimer's disease and senile dementia. Raven, New York, pp 103–120
Newcombe F (1980) Memory: a neuropsychological approach. Trends Neurosci 179–182
Poon LW (1983) Application of information-processing technology in psychological assessment. In: Crook T, Ferris S, Reisberg B (eds) Assessment in geriatric psychopharmacology. Powley, New Canaan, CT
Purish AD, Golden CJ, Hammeke TA (1978) Discrimination of schizophrenia and brain-injured patients by a standardised version of Luria's neuropsychological tests. J Consult Clin Psychol 46:1266–1273
Rossor MN (1982) Neurotransmitters and CNS disease: Dementia. Lancet II:1200-1204
Sternberg S (1966) High speed scanning in human memory. Science 153:652–654
Sternberg S (1975) Memory scanning: new findings and current controversies. Q J Exp Psychol 27:1–32
Strub RI, Black FW (1981) Alzheimer's/Senile dementia. In: Strub RI, Black FW (eds) Organic brain syndromes. Davis, Philadelphia, pp 119–164
Sulkava R, Amberla K (1982) Alzheimer's disease and senile dementia of Alzheimer type: a neuropsychological study. Acta Neurol Scand 65:541–552
Van Praag HM (1982) Depression. Lancet II:1259–1264
Vink M, Jolles J (1985) A new version of the trailmaking test as an information-processing task. J Clin Neuropsychol 7:162
Wing JK, Cooper JE, Sartorius N (1974) Measurement and classification of psychiatric symptoms. Cambridge University Press